

Claims

1. A non-interacting drug combination comprising a HMG-CoA reductase inhibitor, which is (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl] (3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof and a drug which is an inhibitor, inducer or substrate of P450 isoenzyme 3A4.
2. A non-interacting drug combination, as claimed in claim 1, wherein the second drug is an inhibitor or inducer of P450 isoenzyme 3A4.
3. A non-interacting drug combination, as claimed in either claim 1 or claim 2, wherein each drug is administered together or each drug is administered sequentially.
4. A non-interacting drug combination, as claimed in any claim from 1 to 3, wherein the second drug is used to lower cholesterol and is an inducer, inhibitor or substrate of P450 isoenzyme 3A4.
5. A non-interacting drug combination, as claimed in claim 4, wherein the second drug is selected from bezafibrate, clofibrate, fenofibrate, gemfibrozol and niacin.
6. A non-interacting drug combination, as claimed in claim 5, wherein the second drug is fenofibrate.
7. A non-interacting drug combination, as claimed in any claim from 1 to 3, wherein the second drug is used in treating cardiovascular conditions and is also an inhibitor, inducer or substrate of P450 isoenzyme 3A4.
8. A non-interacting drug combination, as claimed in claim 7, wherein the second drug is selected from digitoxin, diltiazem, losartan, nifedipine, quinidine, verapamil and warfarin.

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2nd drug.

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9. A non-interacting drug combination, as claimed in any claim from 1 to 3, wherein the second drug is used in immunosuppression therapy and is an inducer, inhibitor or substrate of P450 isoenzyme 3A4.

10. A non-interacting drug combination, as claimed in claim 9, wherein the second drug is selected from cyclosporin, tacrolimus and a corticosteroid.

11. A non-interacting drug combination, as claimed in any claim from 1 to 10, wherein (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl]

(3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof is dosed at 5, 10, 20, 40 or 80mg once per day.

12. A pharmaceutical formulation comprising (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl] (3R,5S)-3,5-dihydroxyhept-6-enoic acid or a

pharmaceutically acceptable salt thereof, a drug which is an inducer, inhibitor or substrate of P450 isoenzyme 3A4 and a pharmaceutically-acceptable diluent, carrier or adjuvant.

13. A pharmaceutical formulation, as claimed in claim 12, wherein the second drug is a substrate of P450 isoenzyme 3A4 and is selected from acetaminophen, aldrin, aflentanil,

amiodorane, astemizole, benzphetamine, budenoside, carbamazepine, cyclophosphamide, cyclosporin, dapsone, digitoxin, diltiazem, diazepam, erythromycin, etoposide, flutamide, hydroxyarginine, ifosfamide, imipramine, lansoprazole, lidocaine, lovastatin, losartan, lovastatin, midazolam, nifedipine, omeprazole, quinidine, rapamycin, retenoic acid, steroids, tacrolimus, teniposide, theophylline, toremifene, triazolam, troleandomycin, verapamil, warfarin, zatosetron and zonisamide.

14. A pharmaceutical formulation, as claimed in claim 12, wherein the second drug is an inhibitor of P450 isoenzyme 3A4 and is selected from clotrimazole, ethinylestradiol, gestodene, itraconazole, ketoconazole, miconazole, diltiazem, naringenin, erythromycin,

cyclosporin and triacetyloleandomycin.

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15. A pharmaceutical formulation, as claimed in claim 12, wherein the second drug is an inducer of P450 isoenzyme 3A4 is selected carbamazepine, dexamethasone, phenobarbital, phenytoin, rifampin, sulfadimidine, sulfinipyrazone and triacetyloleandomycin.

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16. A pharmacy pack comprising a first drug which is (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl] (3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof and a second drug which is an inducer, inhibitor or substrate of P450 isoenzyme 4A4. 9P

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17. A pharmacy pack, as claimed in claim 16, wherein the second drug is used to lower cholesterol and is an inducer, inhibitor or substrate of P450 isoenzyme 3A4.

18. A pharmacy pack, as claimed in claim 17, wherein the second drug is selected from
15 bezafibrate, clofibrate, fenofibrate, gemfibrozol and niacin.

19. A pharmacy pack, as claimed in claim 16, wherein the second drug is used in treating cardiovascular conditions and is also an inhibitor, inducer or substrate of P450 isoenzyme 3A4.

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20. A pharmacy pack, as claimed in claim 19, wherein the second drug is selected from, digitoxin, diltiazem, losartan, nifedipine, quinidine, verapamil and warfarin.

21. A pharmacy pack, as claimed in claim 16, wherein the second drug is a substrate of
25 P450 isoenzyme 3A4 and is selected from acetaminophen, aldrin, aflentanil, amiodorane, astemizole, benzphetamine, budenoside, carbamazepine, cyclophosphamide, cyclosporin, dapsone, digitoxin, diltiazem, diazepam, erythromycin, etoposide, flutamide, hydroxyarginine, ifosfamide, imipramine, lansoprazole, lidocaine, lovastatin, losartan, lovastatin, midazolam, nifedipine, omeprazole, quinidine, rapamycin, retenoic acid, steroids, tacrolimus,
30 teniposide, theophylline, toremifene, triazolam, troleandomycin, verapamil, warfarin, zatosetron and zonisamide.

22. A pharmacy pack, as claimed in claim 16, wherein the second drug is an inhibitor of P450 isoenzyme 3A4 and is selected from clotrimazole, ethinylestradiol, gestodene, itraconazole, ketoconazole, miconazole, diltiazem, naringenin, erythromycin, cyclosporin and triacetyloleandomycin.

23. A pharmacy pack, as claimed in claim 16, wherein the second drug is an inhibitor of P450 isoenzyme 3A4 and is selected from carbamazepine, dexamethasone, phenobarbital, phenytoin, rifampin, sulfadimidine, sulfinipyrazone and triacetyloleandomycin.

24. Use of (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl] (3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof in the preparation of a medicament for use in combination therapy with a second drug which is an inducer, inhibitor or substrate of P450 isoenzyme 3A4.

25. Use of (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl] (3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof in the preparation of a medicament for use in cholesterol lowering therapy in combination therapy with a second drug which is an inducer, inhibitor or substrate of P450 isoenzyme 3A4.

26. Use, as claimed in claim 25, wherein the second drug is selected from bezafibrate, clofibrate, fenofibrate, gemfibrozol and niacin.

27. Use of (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-[methyl(methylsulfonyl)amino]pyrimidin-5-yl] (3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof in the preparation of a medicament for use in the treatment of cardiovascular condition in combination with a second which is an inducer, inhibitor or substrate of P450 isoenzyme 3A4.

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28. Use, as claimed in claim 27, wherein the second drug is selected from digitoxin, diltiazam, losartan, nifedipine, quinidine, verapamil and warfarin.

VI. 29. Use of (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-
5 [methyl(methylsulfonyl)amino]pyrimidin-5-yl] (3R,5S)-3,5-dihydroxyhept-6-enoic acid or a pharmaceutically acceptable salt thereof in the preparation of a medicament for use in cholesterol lowering therapy in a patient receiving immunosuppressive therapy.

30. Use, as claimed in claim 29, wherein the immunosuppressive therapy comprises the
10 administration of a drug selected from cyclosporin, tacrolimus and a corticosteroid.

31. Use of (E)-7-[4-(4-fluorophenyl)-6-isopropyl-2-
[methyl(methylsulfonyl)amino]pyrimidin-5-yl] (3R,5S)-3,5-dihydroxyhept-6-enoic acid or a
pharmaceutically acceptable salt thereof in the preparation of a medicament for use in
15 cholesterol lowering therapy in combination with a second drug which is selected from bezafibrate, clofibrate, fenofibrate, gemfibrozil and niacin in a patient receiving immunosuppressive therapy.

32. Use as claimed in claim 31 wherein the immunosuppressive therapy comprises the
20 administration of a drug selected from cyclosporin, tacrolimus and a corticosteroid.